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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/211,315	12/14/1998	WILLIAM J. BOYLE	A-451-G	7234

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EXAMINER	
NICHOLS, CHRISTOPHER J	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/211,315	BOYLE, WILLIAM J.	
	Examiner	Art Unit	
	Christopher J Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37, 39-52, and 54-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37, 39-52, and 54-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *37, 39-52, and 54-69* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 December 1998* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3.29.99 10.18.00*. 3/5/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 13 February 2004 has been entered.

Status of Application, Amendments, and/or Claims

2. The Response filed 23 March 2004 has been received and entered in full. The instant application is now in compliance with the requirements of 37 CFR §1.821 through §1.825.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

4. The Objection to the Drawings as set forth at pp. 3-4 ¶8-9 in the previous Office Action (13 August 2003) is hereby *withdrawn* in view of Applicant's amendments (13 February 2004).

5. The Objection to the Specification as set forth at pp. 4 ¶10-13 in the previous Office Action (13 August 2003) is hereby *withdrawn* in view of Applicant's amendments (13 February 2004).

6. The Objections to the claims as set forth at pp. 4-5 ¶14-15 in the previous Office Action (17 January 2003) is *withdrawn* in view of Applicant's amendments (13 January 2004).

7. The Rejection of claims **37** and **52** under 35 U.S.C. §112 ¶2 as set forth at pp. 6-7 ¶16-19 in the previous Office Action (17 January 2003) is *withdrawn* in view of Applicant's amendments (13 January 2004).

8. The Rejection of claims **37-66** under provisional non-statutory double patenting as set forth at pp. 7-8 ¶20-22 in the previous Office Action (17 January 2003) is *withdrawn* in view of Applicant's amendments (13 January 2004).

9. All rejections and objections not maintained or put forth herein are hereby *withdrawn.*

New Objections And/Or Rejections

Specification

10. At pp. 11 lines 28-30, pp. 50 lines 29-30, the address of the American Type Culture Collection (ATCC) is incorrect. Applicant is advised that the address for the ATCC has recently changed, and that the new address should appear in the specification. The new address is:

American Type Culture Collection

10801 University Boulevard

Manassas, VA 20110-2209

11. The specification should be amended to include such, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information.

12. The disclosure is objected to because of the following informalities: misspelling "CHOd-" (pp. 13 line 23). Appropriate correction is required.

13. The disclosure is objected to because of the following informalities: the status of the following US Patent Applications should be updated (pp. 24, 40, 43, 44): "Application No. 08/706,945, now U.S. Patent No. 6,369,027." And "Application No. 08/577,788, now U.S. Patent No. 6,613,544." Appropriate correction is required.

Provisional Obviousness-Type Non-Statutory Double Patenting

14. Claims **37, 39-52,** and **54-66** are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 31-33 of copending Application No. 09/079569 (herein cited as US Patent Application 2003/0104485 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of 09/079569 are directed to a method of treating a bone disease in a mammal comprising administering a therapeutically effective amount of a modulator of an osteoprotegerin binding protein wherein said modulator is an antibody, or fragment thereof, which specifically binds an osteoprotegerin binding protein. Although not identical to the instant claims, the preamble of treating a bone disease is encompassed by the preamble of claim 37 "to

inhibit bone resportion" and claim 52 "to inhibit osteoclastogenesis" and the essential method steps of both 09/079569 and the instant application are to administer a therapeutic antibody or fragment thereof that binds osteoprotegerin binding protein.

15. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the method as detailed in 09/079569 to treat bone disease in a mammal as inhibiting bone resorption and inhibiting osteoclastogenesis will both accomplish a relief of symptoms for bone disease. Also, both applications methods are essentially consist of administering a therapeutic antibody or fragment thereof that binds osteoprotegerin binding protein.

16. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. Applicant traversed this rejection on the grounds of different filing dates. Applicant's argument is not found persuasive. Instantly both applications are pending with overlapping claims and a shared Inventor thus a double patenting rejection is valid.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims **37, 39-52,** and **54-69** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *methods of inhibiting bone resorption in a mammal and/or inhibiting osteoclastogenesis in a mammal comprising administering to said mammal an*

antagonist antibody or fragment thereof which binds an osteoprotegerin binding protein at the epitopes of residues 159-317 of SEQ ID NO: 39, BB' loop-Cys, and EF loop-Cys, does not reasonably provide enablement for *other antibodies, antibodies prepared from immunization of transgenic animals capable of producing human antibodies, other epitopes*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to **make** or **use** the invention commensurate in scope with these claims.

19. The claims are drawn very broadly to methods of using any number of antibodies which bind residues 1 to 317 of SEQ ID NO: 39.

20. The specification teaches that antagonist antibody or fragment thereof which binds an osteoprotegerin binding protein (OBP) at the epitopes of residues 159-317 of SEQ ID NO: 39, BB' loop-Cys, and EF loop-Cys show inhibition of osteoclastogenesis (see also Declaration of John K. Sullivan filed on 21 August 2000).

21. The specification fails to provide any guidance for the successful use of other antibodies or their manufacture/isolation. And since resolution of the various complications in regards to making/isolating an antagonistic antibody with therapeutic activity/value is highly unpredictable, one of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the art as outlined below, the quantity of experimentation required to practice the invention as claimed *in vivo* would require the *de novo* determination of formulations of new anti-OBP antibodies and then screen them for therapeutic activity. In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

22. Additionally, a person skilled in the art would recognize that predicting the efficacy of using any given anti-OBP antibody based solely on the performance of three antibodies is highly problematic (see MPEP §2164.02). Thus, although the specification prophetically considers and discloses general methodologies of using the claimed therapy methods, such a disclosure would not be considered enabling since the state of antibody therapy and OBP, at the time of filing, is highly unpredictable and complex. The factors listed below have been considered in the analysis of enablement [see MPEP §2164.01(a) and *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)]:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

23. On the nature of the invention, while antibodies which bind osteoprotegerin binding protein may constitute a fecund ground for investigation, the CAFC ruled in *Genentech Inc. v. Novo Nordisk A/S* (CA FC) **42 USPQ2d 1001** (1997) that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Citing *Brenner v. Manson,* **383 U.S. 519, 536, 148 USPQ 689, 696** (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). Therefore the CFAC stated that tossing out the mere germ of an idea does not constitute enabling disclosure.

While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. That requirement has not been met in the instant specification with respect to the any give antibody which bind osteoprotegerin binding protein which in turns has therapeutic activity for bone resorption. Only antibodies which antagonist antibody or fragment thereof which binds an osteoprotegerin binding protein at the epitopes of residues 159-317 of SEQ ID NO: 39, BB' loop-Cys, and EF loop-Cys are enabled by the instant Specification.

24. On the state of the prior art, it is silent on OBP and anti-OBP antibody therapies. Therefore no guidance is present for the skilled artisan to make and use the invention as claimed outside what is presented in the instantly filed Specification.

25. Thus the specification of the instant application fails to provide adequate guidance for one of skill in the art to overcome the unpredictability and challenges of making and using antagonistic antibodies which bind osteoprotegerin binding protein.

26. Claims **37, 39-52,** and **54-69** are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

27. The independent claims requires an antagonistic anti-osteoprotegerin binding protein antibody which binds to residues 1 to 317 of SEQ ID NO: 39 while the claims do not specific an epitope nor do the claims require that the antibody's target possess any particular conserved

structure, or other distinguishing feature, such as a sequence. Thus, the claims are drawn to a genus of antibodies that is defined by binding anywhere, anyhow to residues 1 to 317 of SEQ ID NO: 4.

28. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is a recitation of desired target specificity for the antibody in question. The specification does not identify any particular portion of the target (residues 1 to 317 of SEQ ID NO: 39) that must be conserved, nor does it provide an epitope. The distinguishing characteristics of the claimed genus are not described. Accordingly, the specification does not provide adequate written description of the claimed genus.

29. To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563; see also *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); *In re Gosteli*, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement

"by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572.

30. In *Randolph J. Noelle v Seth Lederman, Leonard Chess and Michael J. Yellin* (CAFC, 02-1187, 20 January 2004) the CAFC held that "Therefore, based on our past precedent, as long as an applicant has disclosed a "fully characterized antigen," either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen.

31. Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application. Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another

unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application.

a. Moreover, Noelle cannot claim the genus form of CD40CR antibody by simply describing mouse CD40CR antigen."

32. Therefore the full breadth of the claim fails to meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

33. Claims **43** and **58** are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

34. The claims require that the antibodies used in the claimed methods be "prepared by immunization of a transgenic animal capable of producing human antibodies" while no such animal existed at the time of the filing of the instant Specification. Thus the hypothetical animal must be made.

35. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is a recitation of known methods of making antibodies excluding

preparation by immunization of a transgenic animal capable of producing human antibodies. The specification does not identify any particular portion of the structure that must be conserved, nor does it provide a disclosure of structure/function correlation. The distinguishing characteristics of the claimed genus are not described. Accordingly, the specification does not provide adequate written description of the claimed genus.

36. To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563; see also *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); *In re Gosteli*, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572.

37. See *University of Rochester v. G.D. Searle & Co.*, 68 USPQ2d 1424 (DC WNY 2003) and *University of Rochester v. G.D. Searle & Co. et al.* CAFC [(03-1304) 13 February 2004]. In *University of Rochester v. G.D. Searle & Co.* a patent directed to method for inhibiting prostaglandin synthesis in human host using an unspecified compound, in order to relieve pain without side effect of stomach irritation, did not satisfy written description requirement of 35

U.S.C. §112, since the patent described the compound's desired function of reducing activity of the enzyme PGHS-2 without adversely affecting PGHS-1 enzyme activity, but did not identify said compound, since invention consists of performing "assays" to screen compounds in order to discover those with desired effect. The patent did not name even one compound that assays would identify as suitable for practice of the invention, or provide information such that one skilled in art could identify a suitable compound. And since specification did not indicate that compounds are available in public depository, the claimed treatment method cannot be practiced without the compound. Thus the inventors cannot be said to have "possessed" the claimed invention without knowing of a compound or method certain to produce said compound. Thus said patent constituted an invitation to experiment to first identify, then characterize, and then use a therapeutic a class of compound defined only by their desired properties.

38. Therefore the full breadth of the claim fails to meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

Summary

39. No claims are allowed.

40. The following articles, patents, and published patent applications were found by the Examiner during the art search while not relied upon for the instant rejection(s) are considered pertinent to the instant application:

b. US 6,645,500 B1 (11 November 2003) Halker & Haaning

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is **(571) 272-0889**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback** can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Elizabeth C. Kemmerer

CJN
October 7, 2004

ELIZABETH KEMMERER
PRIMARY EXAMINER